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Malaria in Pregnancy

TL MAGWALI

Introduction

It is estimated that nearly five billion episodes of clinical malaria occur worldwide each year. The disease causes about three million deaths annually with Africa suffering 90% of this burden.¹ It is also estimated that 25 million women fall pregnant in the malaria-endemic areas of Africa each year.² Most of the deaths due to malaria in Africa are in pregnant women and children under the age of five years.³

Plasmodium falciparum causes the most severe malarial illness and most cases in Africa are caused by this species of the malaria parasite.³ The prevalence of *Plasmodium falciparum* infection among pregnant women in rural areas in parts of Africa can be very high. Verhoff and co-workers found a prevalence of *plasmodium falciparum* malaria of 35.3% among *primigravidae* and 13.6% in *multigravidae* in a study done among pregnant women in rural Malawi.⁴

Women who live in areas of high or moderate (stable) malaria transmission have a degree of immunity to malaria whereas women who live in areas of low (unstable) malaria transmission usually have no immunity to the disease.⁵

Pregnancy is known to cause a lowered capacity for type 1 immune response.⁶ This reduces immunity to diseases such as malaria, tuberculosis and leishmaniasis.

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Effect of Pregnancy on Malaria.

Women who live in malaria endemic areas may have an asymptomatic background parasitaemia. This asymptomatic parasitaemia can be punctuated by episodes of acute febrile illness due to malaria. The incidence of these episodes of febrile illness due to malaria increases during pregnancy especially in *primigravidae* and the duration of illness may be significantly longer.⁷

Pregnant women, especially those living in areas of low or unstable transmission, are more likely to suffer from the severe complications of Malaria compared to non-pregnant individuals living in the same area. These complications include cerebral malaria, hypoglycaemia, pulmonary oedema and severe haemolytic anaemia.^{8,9}

Effect of Malaria on Pregnancy.

Malaria parasites have a high affinity for the decidual cells of the placenta. The intervillous spaces may be heavily parasitized with a heavy presence of

macrophages.¹⁰ In a study done among 1 177 rural women in Tanzania, evidence of malaria infection was found in 75.5% of placental samples.¹¹ The incidence of the malarial parasite actually crossing the placenta (congenital malaria) is low, however, and is quoted at around 3%.¹² Heavy parasitization of the placenta may lead to impaired nutrient and oxygen transfer to the growing foetus. This leads to an increased risk of miscarriage and premature labour in women who have suffered malaria during pregnancy.^{13,14}

Another possible consequence of placental malaria is intra-uterine growth restriction and subsequent low birth weight. Malaria in pregnancy is estimated to contribute eight to 14% low birth weight babies in endemic areas.² Women who have suffered malaria during pregnancy have a higher stillbirth rate.¹³

A complication of the acute or chronic haemolysis, that occurs in malaria is anaemia. Malaria contributes three to 15% of severe anaemia cases in pregnant women in endemic areas.²

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Malaria in Pregnancy and HIV Infection.

Immunity to malaria can be further reduced in women who are HIV positive. The prevalence and severity of malaria in pregnancy have been shown to be higher in HIV positive women. The parasite density, prevalence of anaemia and incidence of cerebral malaria are all higher in HIV positive compared to HIV negative women. The efficacy of sulfadoxine/pyrimethamine (SP) in reducing placental parasitaemia has been shown to be impaired.^{15,16}

Diagnosis.

It is worth noting that the clinical features of malaria may be atypical in pregnancy, for example the fever may not follow the usual remittent pattern. In some cases maternal anaemia may be the only presenting feature especially in *multigravidae*.³

Treatment of Malaria During Pregnancy.

Plasmodium falciparum has shown resistance to chloroquine in most areas of Africa.^{17,18} Use of a combination of Artemether and Lumefantrine for the treatment of malaria was shown to be more cost-effective than using chloroquine and Sulfadoxine/pyrimethamine (SP). Widespread use of the Artemether/Lumefantrine combination may be limited by lack of resources in most parts of Africa.¹⁸

Malaria in pregnancy can be treated with oral quinine 600mg six hourly for seven days followed by clindamycin 300mg orally six hourly for five days. Doxycycline cannot be used as the follow-up treatment to Quinine as use of the former is contra-indicated during pregnancy. In very ill patients Quinine 20mg/kg can be given as a loading dose followed by 10mg/kg over four hours given eight hourly. The loading and maintenance doses are all given as infusion. The maintenance dose is continued until the patient can take orally.¹⁹

Artemisinin derivatives may be used in pregnancy when benefits outweigh the risks. Their use is not recommended in the first trimester. WHO advocates the use of artemisinin derivatives in combination with other drugs (artemisinin based combination therapies ACT's). Coartem is a combination of artemether and lumefantrine. It is given in a dose of four tablets twice daily for three days.¹⁹

Benign Forms of Malaria

Plasmodium vivax, *ovale* and *malariae* are still largely sensitive and will respond to a standard dose chloroquine. The hypnozoites (dormant liver forms) of *Plasmodium vivax* and *Plasmodium ovale* are treated with primaquine. Primaquine is contra-indicated during pregnancy as it may possibly cause haemolysis in the foetus. In cases of *Plasmodium vivax* or *ovale* infection during pregnancy, the patient should be given chloroquine 600mg weekly until delivery after she has completed the standard dose of treatment. Primaquine is then given after delivery in a dose of 30mg once daily for 30 days in case of *vivax* infection and 15mg daily for

30 days in the case of *malariae* infection.¹⁹

Prophylaxis.

Pregnant women travelling from non-endemic to endemic areas need prophylaxis against malaria. Such travel should be discouraged unless it is absolutely necessary. If at all possible, such travel should ideally be undertaken after the first trimester. As prophylaxis, a combination of pyrimethamine and dapsone should be given once a week starting two weeks before entering the malarious area, continuing whilst in the area and continuing for four weeks after leaving the area. Folic acid supplementation should be given when this prophylaxis is given.¹⁹

Intermittent Preventive Treatment.

WHO recommends Intermittent Preventive Treatment (IPT) as one of the strategies against malaria in pregnancy in women who live in endemic areas. The other two are use of insecticide treated nets (ITN's) and effective case management. IPT involves the giving of a total of three doses of SP at intervals of at least one month apart. The IPT is started soon after the first trimester and after when the first movements are felt. Supplementation with ferrous sulphate and folate should also be given to all pregnant women who live in endemic areas. For endemic areas, WHO also recommends spraying programmes and continuing medical education to health professionals who work in malaria endemic areas.³

IPT has been shown to reduce the prevalence of anaemia in women living in endemic areas and to reduce the incidence of low birth weight.⁴ The benefits of IPT with SP may soon be undermined by increasing levels of resistance to SP. Research on several candidate alternative combinations is on-going.²⁰

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